

APPLICANTS: Hopkins et al.  
SERIAL NUMBER: 10/722,279

### **REMARKS**

Examination of claims 21-47 is reported in the present Office action. Claims 21-47 stand rejected under 35 U.S.C. § 112, second paragraph. Claims 21-47 stand rejected under 35 U.S.C. § 102(e) and claim 44 stands rejected under 35 U.S.C. § 103(a). The specification and claims 23, 24, 46, and 47 are further objected to. Each of these rejections and objections is addressed below.

#### **New Claims**

Support for new claims 48-51 is found, for example, in originally filed claims 1, 5, 19, and at page 1, line 27 through page 2, line 2, page 3, lines 24-28, and page 4, lines 3-6. No new matter is added by this amendment.

#### **Objection to the Specification**

As requested by the Office, the specification has been amended to update the priority claim.

#### **Objections to the claims**

Applicants have amended claims 23, 24, 46, and 47 as requested by the Office to correct informalities.

#### **Rejections under 35 U.S.C. § 112, second paragraph**

Claims 21-47 stand rejected for indefiniteness. The Office notes, for example, that it is unclear how the use of “matrix” in claim 21 would end up having the structure of a heart valve.

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Applicants direct the Office's attention to page 6, lines 23-24 which states: "[t]he structure is acellular is acellular and has the geometry of a native cardiac valve." Accordingly, one skilled in the art would immediately recognize how the claimed matrix would assume the configuration of a heart valve. Applicants request withdrawal of this rejection.

The Office further states that the terms "said centrifugal heart valve" in claim 22, "the factors" in claim 28, and "the intended recipient" in claim 39 and 40 lack antecedent basis. Applicants have amended claims 22, 28, 39, and 40 to clarify the claim language. Applicants respectfully request that this aspect of the rejection be withdrawn.

#### Rejections under 35 U.S.C. § 102(e)

Claims 21, 22, 26, 28-36, and 41-44 stand rejected as being anticipated by Goldstein et al. (U.S. Patent No. 5,899,937; hereinafter 'Goldstein').

Amended claim 21, from which the other rejected claims depend, is directed to a method of manufacturing a cellularized bioprosthetic heart valve containing isolated myofibroblasts and isolated endothelial cells. Goldstein only goes so far as to teach a method of manufacturing a heart valve using fibroblasts (e.g., dermal myofibroblasts), and therefore, fails to describe all the features of the claimed method. In fact, Goldstein states at column 6, lines 45-57:

The selection of the dermal fibroblast as the repopulating cell type was chosen because: 1) it is accessible in a potential valve recipient; 2) biochemically, this cell synthesizes types I, III:, and V collagens in the same proportions (85:15:5) as are present in the heart valve leaflet (22)) and synthesizes proteoglycans (1,23) which are apparently important in reducing bending stress in the leaflets (2); and 3) *endothelial cells do not seem to be necessary to prevent thrombus formation in cryopreserved aortic or pulmonary valves and they synthesize type IV collagen, the basement membrane collagen, which does not have a role as a structural protein.* (emphasis added)

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Thus, because Goldstein fails to describe seeding with isolated myofibroblasts and isolated endothelial cells as now claimed, Applicants respectfully request that this aspect of the rejection be withdrawn.

Claims 21-43 and 45-47 also stand rejected as being anticipated by Wolfinbarger et al. (U.S. Patent No. 6,432,712; hereinafter 'Wolfinbarger'). Applicants respectfully submit that Wolfinbarger is not prior art under 35 U.S.C. §102(e), since the claimed invention was conceived by Applicants prior to the effective date of the reference. Submitted with this response is a Declaration under 37 C.F.R. §1.131 executed by Dr. Richard A. Hopkins and Dr. Diane Hoffman-Kim, both inventors in the above-referenced patent application. The Declaration of Dr. Hopkins and Dr. Hoffman-Kim establishes invention of the subject matter of the pending claims prior to the effective date of Wolfinbarger. Thus, Wolfinbarger is not § 102(e) prior art. Therefore, this rejection should be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claim 44 stands rejected as being obvious over Wolfinbarger. As indicated above, Wolfinbarger is not prior art and therefore, this rejection should be withdrawn.

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### CONCLUSION

Applicants submit that the claims are now in condition of allowance and such action is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Enclosed is a petition of extension of time and a check in the amount of the required fee. The Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311 (Reference No. 21486-027DIV).

Respectfully submitted,

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